

Assessment of Prognosis of Acute Pancreatitis on Admission: Comparison of HAPS and APACHE II Scoring Systems

Nigil Abdul Jalal¹

¹(Department of General Surgery, Kasturba Medical College Mangalore, India)

Corresponding Author: Nigil Abdul Jalal

Abstract: Acute pancreatitis is a common and potentially lethal inflammatory process with a highly variable clinical course. Persistent organ failure develops in 10%–20% of patients, with mortality reaching 30% in this subgroup. Since the morbidity and mortality of acute pancreatitis differ markedly between mild and severe disease (mild < 5% vs severe 20–25%), the ability to identify patients at risk for persistent organ failure early in the disease course is very critical, both for triaging patients to the appropriate level of care and for designing mechanistic studies for targeted intervention. Our study aims to assess the severity of acute pancreatitis using APACHE II and HAPS (Harmless Acute Pancreatitis Score) scoring systems, to compare HAPS and APACHE II scoring systems for assessment of prognosis of acute pancreatitis on admission and to assess the feasibility of HAPS scoring system over the complicated APACHE II scoring system. This prospective observational study was conducted on admitted patients clinically suspected to have acute pancreatitis in a tertiary teaching hospital between October 2015 to September 2017. A total of 80 patients were included in the study. Scoring was done on admission or at the time of diagnosis. The scores were compared with the clinical severity which were graded according to Atlanta criteria and also compared with the clinical outcome of the patient. Statistical analysis was done using independent t test. A “p” value of less than 0.05 was considered to be statistically significant. Of the 80 patients studied, 58 (72.5%) patients were positive for HAPS at the time of admission, while 57 (71.25%) patients had an APACHE II score of less than or equal to 8 within 24 hours of admission, signifying uncomplicated mild acute pancreatitis, while eventually 55 (68.8%) patients were found to have a mild course of the disease. As all the indices of statistical power were found to be the more or less the same for both HAPS and APACHE II scores, HAPS is as efficacious as APACHE II scoring system for identifying patients with mild course of the disease at the time of admission, while having the added advantages of being significantly less time-consuming, cumbersome and less invasive and at the same time accurately triaging patients as per disease severity. This indicates that HAPS is capable of identifying the patients who could be reliably triaged to receive less aggressive treatment, making it an ideal predictor for Indian patients at the community level.

Keywords: APACHE II, HAPS, pancreatitis, amylase

Date Of Submission: 15-09-2018

Date of acceptance: 03-10-2018

I. Introduction

Acute pancreatitis refers to the inflammatory process of the pancreas which has a highly variable clinical course¹. Persistent organ failure develops in 10%–20% of patients, with mortality reaching 30% in this subgroup. Between either end of the spectrum of the disease, mild to severe, the risk of complications leading to severe morbidity and mortality grossly changes (mild < 5% vs severe 20–25%), and hence to handpick patients who are at risk for developing organ dysfunction assumes paramount importance, for categorizing patients for administering appropriate care and for adopting management protocols with pinpoint intervention².

The importance of multidisciplinary early aggressive treatment of this inflammatory process of the pancreas is becoming increasingly evident over the past several years. An important prerequisite for effective prevention of adverse outcomes is to selectively intervene early on in the disease course, on those patients who might be prone to develop severe acute pancreatitis. Even though much has been understood on the molecular mechanisms of the disease from experimental models, the struggle to identify an ideal early clinical predictor of severity is still on. An ideal marker for assessing disease status should be simple and uncomplicated, cheap, repeatable and feasible across all levels, from primary to tertiary healthcare³. Several multi- and single-parameter severity predictors, namely acute physiology and chronic health evaluation II (APACHE II) score, Ranson’s score, bedside index of severity of acute pancreatitis (BISAP), systemic inflammatory response syndrome (SIRS) score, procalcitonin, computed tomography severity index (CTSI), blood urea nitrogen (BUN), C-reactive protein (CRP), serum creatinine, and d-dimer have been studied so far³. Of these, barring BUN none fulfils the criteria of an ideal predictor. In the context of BUN, a dynamic increase over 24–48 h of

admission has been shown to predict infected pancreatic necrosis⁴ and in-hospital mortality^{5,6}. As a result of inadequate availability of predictors that could identify the high-risk patients early on, many of the patients with even mild disease (which is seen in 75 % to 80 %) tend to get over-zealous aggressive treatment. It would therefore be desirable to have a simple predictor that evaluates multiple dimensions of the illness and predict clinical outcomes within the first 12–24 h of onset of AP.

Recently, a simple system called the harmless acute pancreatitis score (HAPS) was introduced based on a large prospective study with a sample size of 394 patients from Luneberg Municipal Clinic, Germany⁷. The goal of this system was to identify the patients who would run a non-severe (mild) course of AP. In the study, HAPS could identify the patients who would have a mild disease with a positive predictive value of 98 % (92 % to 100%) within approximately 30 min of admission. Moreover, even a non-specialist can run this system, and it requires a very basic laboratory set up. HAPS could have significant utility compared to other severity predictors in triaging patients with acute pancreatitis in an Indian set up, where predominantly such patients are managed in primary and community-based healthcare setting.

Among the initial attempts at assessing disease severity in patients admitted to ICU was the APACHE scoring system, devised by Knaus et al in the year 1981 which was modified in the year 1985, the APACHE II scoring system^{8,9}. Though not specific for pancreatitis, it has been shown to be reliable. The system consists of twelve variables, and also age, existing co-morbidity and the Glasgow Coma Score, and its merit lies in its ability to monitor treatment response¹⁰. The variables are, heart rate, mean arterial pressure, pH, serum sodium, potassium and creatinine values, body temperature, respiratory rate, oxygenation, hematocrit, white blood cell counts and GCS over a 24 hour period^{10,11}. Five extra points are given to patients, as per APACHE II who require surgery on emergency basis or those with long standing organ dysfunction and two points for stable patients who require elective surgery¹². The APACHE II scoring system can provide an objective assessment to categorize patients with the disease as mild, complicated and fatal¹³.

II. Material And Methods

This prospective comparative study was carried out on patients of the Department of General Surgery at hospitals attached to Kasturba Medical College Mangalore, Karnataka, India from October 2015 to September 2017. A total of 80 adult subjects (both male and females) of age ≥ 18 years were considered for this study.

Study Design: Prospective observational study

Study Location: This was a tertiary care teaching hospital based study done in the Department of General Surgery, at hospitals attached to Kasturba Medical College Mangalore, Karnataka, India.

Study Duration: October 2015 to September 2017.

Sample size: 80 patients (with 95% confidence level).

Statistical analysis: Fischer's exact test, Chi square test, p value < 0.05 considered to be significant.

Inclusion criteria:

1. All patients admitted to the study setting in the study period with acute pancreatitis
2. Either sex
3. Aged ≥ 18 years
4. Serum amylase levels more than thrice the upper limit of normal.
5. Imaging evidence suggestive of acute pancreatitis.

Exclusion criteria:

1. Serum amylase levels below thrice the upper limit of normal.
2. No imaging evidence of acute pancreatitis.

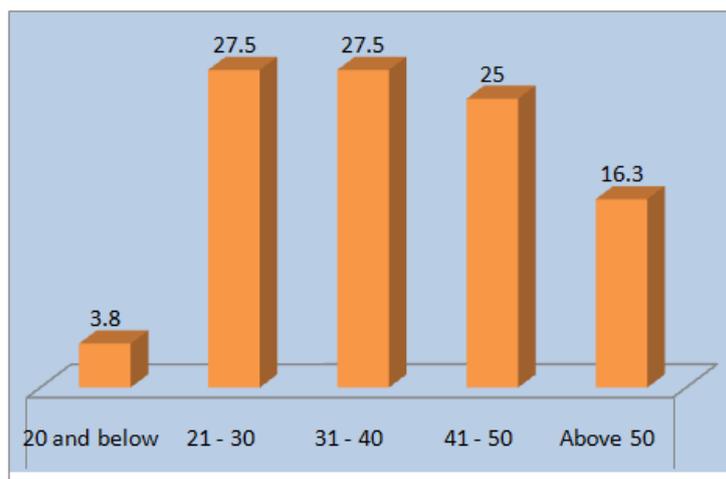
Procedure methodology

HAPS and APACHE II scoring were done on admission or at the time of diagnosis for patients admitted with acute pancreatitis. The scores were compared with the clinical severity which was graded according to Atlanta criteria and also compared with the clinical outcome of the patient.

III. Result

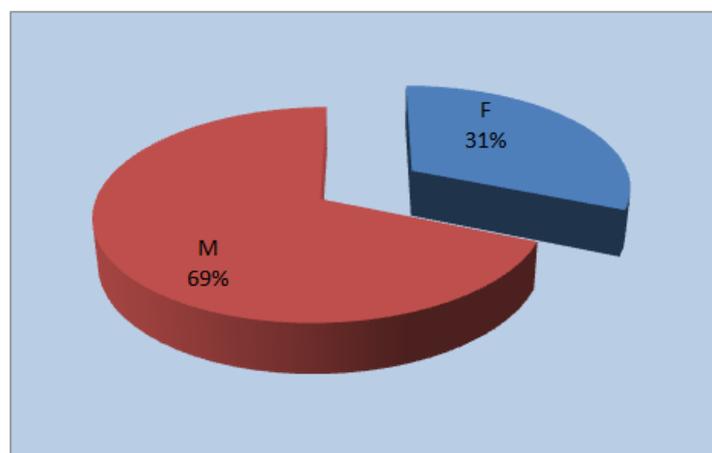
The study was conducted in hospitals attached to Kasturba Medical College Mangalore from October 2015 to September 2017. The sample size was 80. As per Atlanta criteria, 55 patients (68.8%) were classified as Mild Acute Pancreatitis and 25 (31.3%) patients were classified as Severe Acute pancreatitis. Out of 80 patients, 58 patients had a positive HAPS score, while 22 patients had a negative HAPS score. Out of 80 patients, 57 patients had an APACHE II score of less than or equal to 8, while 23 patients had an APACHE II score of greater than 8.

Age Distribution



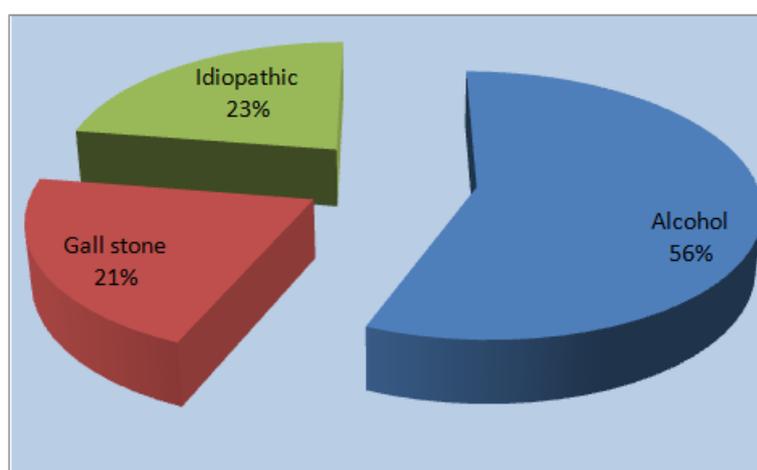
The incidence of acute pancreatitis in the study population was the highest in the 3rd and 4th decades. There was no statistical significance of age ($p=0.963$) on the severity of acute pancreatitis.

Sex Distribution



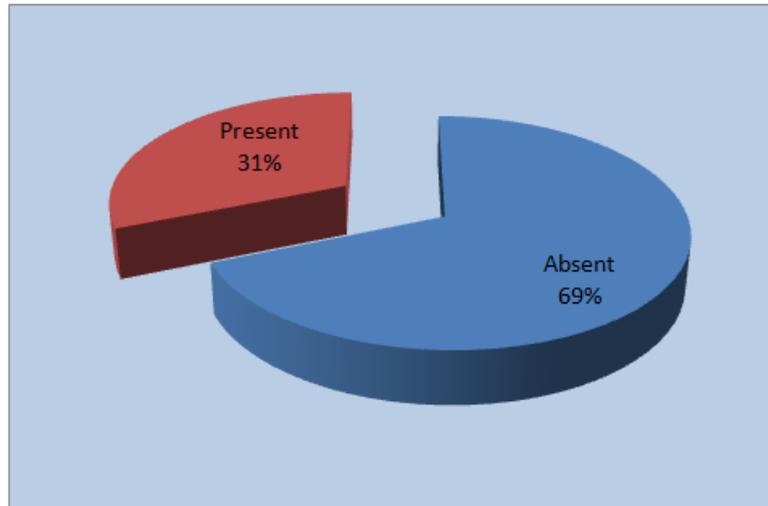
The study population consisted of 55 males (68.8%) and 25 females (31.3%). There was no statistical significance of gender ($p=0.672$) on the severity of acute pancreatitis. However 24% females (6) were surgically managed for the disease as opposed to only 7.3% males (4) who underwent surgery, which was statistically significant ($p=0.045$).

Etiology



Out of the 80 patients, 45 (56.3%) had alcohol induced acute pancreatitis, 17 (21.3%) had gall stone induced acute pancreatitis and 18 (22.5%) had idiopathic acute pancreatitis. The relation between the etiology of the disease with the scoring system was statistically significant ($p=0.009$ with APACHE scoring system and $p = 0.028$ with HAPS scoring system).

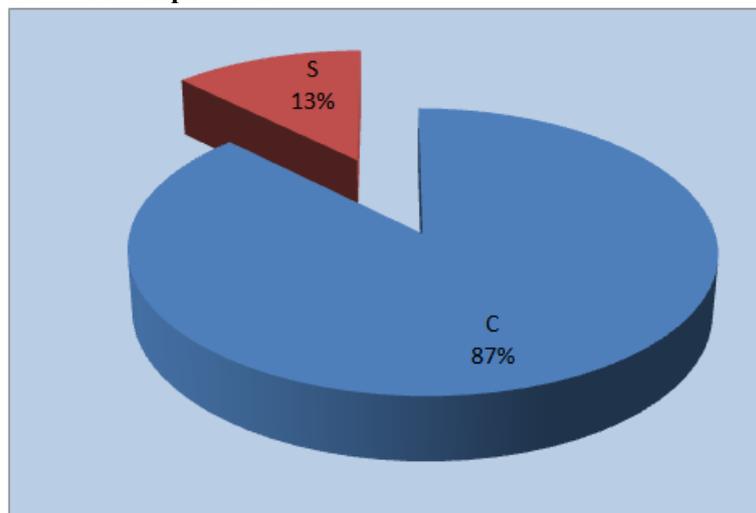
Outcome of patients



Out of the 80 patients with acute pancreatitis, 55 patients (69%) had an uncomplicated outcome. 25 patients (31%), out of the study sample, developed complications, of which 23 patients (92%) developed local complications while 2 patients (8%) developed systemic complications. Among the patients who developed local complications, 11 had pancreatic pseudocyst, 8 had pancreatic necrosis, and 4 patients developed hemorrhagic pancreatitis. Systemic complications developed in 2 patients with SIRS, who eventually expired.

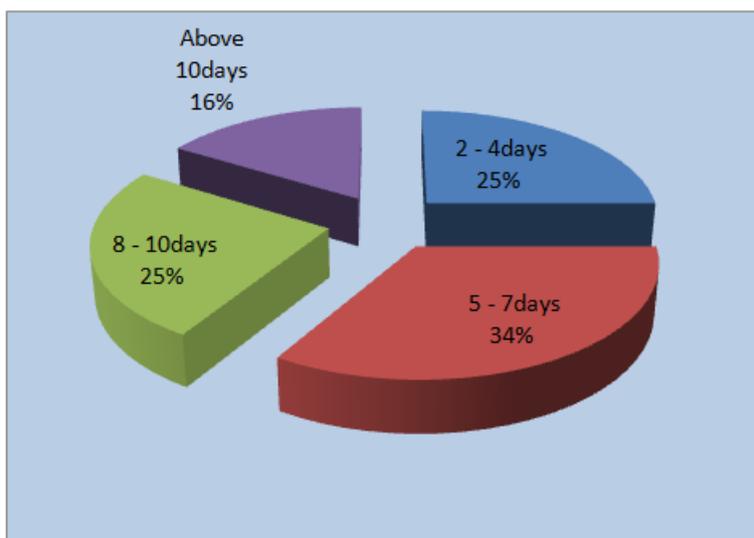
All the patients who had developed complications had negative HAPS score and significantly higher APACHE II scores than those with mild acute pancreatitis ($p<0.001$).

Management of patients with complications



Surgical intervention was carried out in 10 patients, 7 patients had undergone cholecystectomy for gall stone induced pancreatitis, 2 patients had undergone cystogastrostomy for pancreatic pseudocyst while 1 patient had undergone necrosectomy for pancreatic necrosis.

Hospital stay



The mean duration of hospital stay for patients with mild acute pancreatitis was 6.2 days while that for patients with the severe disease was 10.8 days. The duration of hospital stay was not statistically significant.

Prediction of severity of acute pancreatitis by APACHE II score and HAPS score

1) **APACHE II Score**

Severity by APACHE II	Frequency	Percentage
Severe (More than 8)	23	28.75
Mild (Less than 8)	57	71.25
Total	80	100.0

			APACHE II Score		Total	
			More than 8	Less than 8		
ATLANTA	SEVERE	COUNT	23	2	25	
		% within Atlanta	92.0%	8.0%	100.0%	
		% within APACHE II	100.0%	0.0%	31.3%	
	MILD	COUNT	0	55	55	
		% within Atlanta	0%	100.0%	100.0%	
		% within APACHE II	0%	96.5%	68.8%	
			COUNT	23	57	80
			% within Atlanta	28.75%	71.25%	100.0%
			% within APACHE II	100.0%	100%	100.0%

	Estimate	Confidence Interval	
		Lower	Upper
Sensitivity	92.00	81.37	102.63
Specificity	96.36	91.42	101.31
PPV	92.00	81.37	102.63
NPV	96.36	91.42	101.31
Overall accuracy**	95.00	90.22	99.78
	Value	p=	
Kappa	0.884	0.000	HS

In the study, an APACHE II score of more than 8, had correctly identified 23 out of 25 cases of severe acute pancreatitis within 24 hours of admission, with a 92% sensitivity and 96.3% specificity in identifying severity of the disease, while being statistically highly significant. APACHE II score had an overall accuracy of 95 % in the determination of severity of the disease

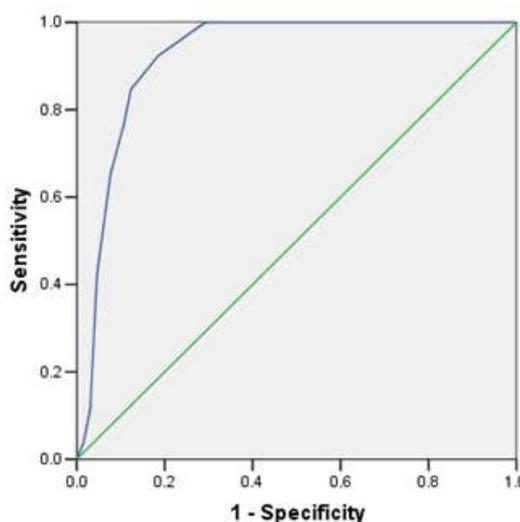
2) HAPS Score

Severity by HAPS	Frequency	Percentage
Severe (Negative)	22	27.5
Mild (Positive)	58	72.5
Total	80	100.0

			HAPS Score		Total
			Positive	Negative	
ATLANTA	SEVERE	COUNT % within Atlanta % within HAPS	22 88.0% 100.0%	3 12.0% 0.0 %	25 100.0% 31.3%
	MILD	COUNT % within Atlanta % within HAPS	0 0% 0%	55 100.0% 96.5%	55 100.0% 68.8%
		COUNT % within Atlanta % within HAPS	22 27.5% 100.0%	58 72.5% 100%	80 100.0% 100.0%

	Estimate	Confidence Interval	
		Lower	Upper
Sensitivity	88.00	75.26	100.74
Specificity	94.55	88.54	100.55
PPV	88.00	75.26	100.74
NPV	94.55	88.54	100.55
Overall accuracy**	92.50	86.73	98.27
	Value	p=	
Kappa	0.825	0.000	HS

ROC Curve



Diagonal segments are produced by ties.

In the study, HAPS scoring system had correctly identified 22 out of 25 patients with severe acute pancreatitis, at the time of admission, with a sensitivity of 88 % and specificity of 94.6 % in identifying the severity of the disease. HAPS had an overall accuracy of 92.5 % in the determination of severity of the disease. Receiving operator characteristics AUC (Area under the curve) for HAPS as a predictor was 92.2 (86.7 to 97.7). Both APACHE II and HAPS scores had 100 % sensitivity in identifying patients with systemic complications.

IV. Discussion

In the present study, an attempt at validating the utility of Harmless Acute Pancreatitis Score (HAPS) for patients in Indian setting, directly admitted with acute pancreatitis, has been made, by comparing it with the well tested and established APACHE II score. Lankisch et al had first proposed HAPS in 2009 on the basis of results of a prospective study with a cohort of 394 patients, in the Luneberg Municipal Clinic, Germany.

In the study by Lankisch et al, HAPS had well predicted mild (non severe) course of acute pancreatitis with a specificity of 97% and positive predictive value of 98%.

The study was reattempted in Sweden in 2011, from a cohort of 511 patients, where HAPS could predict a mild course of disease with a positive predictive value of 98.7% and specificity of 96%¹⁴.

The downside of the original study by Lankisch et al was the exclusion of interventions, an attempt at which has been made here¹⁵.

In this study, the cumbersome APACHE II scoring system is compared with the simple and significantly less time consuming HAPS scoring system. The severity of acute pancreatitis has been classified based on the Atlanta criteria.

Eventual clinical outcomes, duration of hospital stay, interventions and in-hospital mortality were analysed in the study. No adverse systemic outcomes were seen in patients who fulfilled the HAPS criteria as well as those with less-than-eight APACHE II mean score.

Acute pancreatitis was found to be 2.2 times more common in males than in females. Alcohol was the etiological factor in 56.3% of patients and gall stones in 21.3%, contrary to the findings by Larvin et al in which alcohol was causative in 22% and gall stones in 43%. The final outcome of the disease does not depend much on the etiology which might suggest that once the pathogenic mechanisms have been initiated, the course and outcome are not influenced by the etiological factors.

Coming to severity, as determined by the Atlanta criteria, 55 patients (68.5%) had mild acute pancreatitis while 25 patients (31.25%) had severe acute pancreatitis. Larvin et al had 20% of the study population having severe acute pancreatitis. Mortality in the study was 2.5% which was less than that by Larvin et al (7.5%).

APACHE II Score	Larvin et al ¹⁶	Present study
Sensitivity	71%	92%
Specificity	91%	96.4%
Positive Predictive Value	67%	92%
Negative Predictive Value	93%	96.4%
Accuracy	87%	95%

In the study, 22 out of 25 patients who eventually had severe acute pancreatitis had a negative HAPS score which corresponded to higher mean APACHE II scores. The mean APACHE II score was 5.2 for mild acute pancreatitis cases and 12.3 for severe acute pancreatitis cases. However APACHE II had detected 23 out of 25 patients who had an eventual severe course of the disease.

Comparing outcomes in patient groups with the severe and mild disease, it was observed that local complications like pancreatic necrosis and hemorrhagic pancreatitis, and systemic complications including major organ failure were found in patients with a negative HAPS score and mean APACHE II score exceeding 8.

In the study, a negative HAPS score and APACHE II score of more than 8 had the highest sensitivity, specificity and accuracy for the prediction of severity in acute pancreatitis.

HAPS had a sensitivity of 88% and specificity of 94.6% as opposed to APACHE II with 92% and 96.4% respectively in the study. While APACHE II scoring system had an overall accuracy of 95% in detecting patients with the mild course acute pancreatitis, within 24 hours of admission, the same was achieved by HAPS with an overall accuracy of 92.5% but with drastically reduced time consumption of within an hour of admission of the patient.

Scoring system	Sensitivity	Specificity	PPV	NPV	Accuracy
HAPS	88%	94.6%	88%	94.6%	92.5%
APACHE II	92%	96.4%	92%	96.4%	95%

From this study, it is evident that HAPS scoring system has more or less comparable indices of statistical power with respect to APACHE II scoring system. Comparing these figures with the study by Lankisch et al in Germany, HAPS had accurately identified patients with mild acute pancreatitis with a specificity of 97% and positive predictive value of 98%.

The study indicates that HAPS scoring system is capable of identifying patients who could be reliably triaged to receive less aggressive management, rapidly. Despite existing evidence based practice guidelines, in actual clinical practice, it is being seen that even for mild cases of acute pancreatitis, treatment like prolonged nil per oral status, use of medications like octreotide and instituting higher generation antibiotics are being carried out. Such practices are currently neither encouraged nor recommended, and occasionally can cause more harm than good, in addition to increasing the financial burden on the patient and the caregiver. Thus, HAPS scoring system helps to efficiently filter out the major bulk of patients with acute pancreatitis who need not be managed overzealously and at times, irrationally.

V. Conclusion

In conclusion, the study attempted to validate the utility of HAPS scoring system for directly admitted patients with acute pancreatitis, in Indian setting, by comparatively analysing it with the well established, though much cumbersome and difficult to follow APACHE II scoring system. Though several severity predictors have been tried and tested to predict adverse outcomes in acute pancreatitis, none so far can match the simplicity or the time efficacy (within an hour of admission) while at the same time, maintain accuracy, of evaluation of severity of acute pancreatitis by HAPS score, making it a potentially ideal indicator.

It is to be emphasized that there is need to validate the HAPS severity assessment system at the community level in a multicentre setting with a larger sample size. Having stated so, HAPS to a great extent, is capable of identifying the patients who could be reliably triaged to receive less aggressive treatment, making it a potentially ideal and efficient predictor, when compared to the other existing prognostication systems, for Indian patients at the community level.

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Nigil Abdul Jalal, " Assessment of Prognosis of Acute Pancreatitis on Admission: Comparison of HAPS and APACHE II Scoring Systems " *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, vol. 17, no. 9, 2018, pp 11-18.